R E M A R K S

Applicants have considered the outstanding official action. It is respectfully submitted that all the claims are directed to allowable subject matter as set forth below.

Claim 13 is rejected under 35 U.S.C. §112, first paragraph, based on the use of the term "highly" in the phrase "highly non-uniform". Claim 13 has been amended to delete the term "highly".

Claims 9 and 12 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. As to claim 9, the Examiner states that the phrase "the electrode" should read "the electrode array". As to claim 12, the Examiner requests clarification as to the claim specifying that the ultrasonic vibration and the varying electric field are applied in different planes.

Claim 9 has been amended in accordance with the Examiner's remarks. Claim 12 has been canceled. Accordingly, the rejection under 35 U.S.C. §112, second paragraph, has been overcome.

Claim 9 is stated to be allowable if rewritten in independent form and to overcome the 35 U.S.C. §112, second paragraph, rejection.

Claim 9 has been rewritten in independent form and the §112 matter addressed as set forth above. Formal allow-

ance of claim 9 is accordingly requested.

Claim 14 is stated to be allowable if rewritten in independent form and to overcome the 35 U.S.C. §112, first paragraph, rejection of the base claim 13.

Claim 14 has been rewritten in independent form and the §112 matter addressed as set forth above. Formal allowance of claim 14 is requested.

The outstanding rejections based on art are as follows:

(1) Claim 12 under 35 U.S.C. §102(b) over SU 744,285 (SU'285) or WO 98/04355 A1 (WO'355);

(2) Claims 1-8, 10-11, 13 and 15 under 35 U.S.C. §103(a) over SU'285 or WO'355 in view of U.S. Reissue Patent No. 33,524 (Schram);

(3) Claim 11 under 35 U.S.C. §103(a) over SU'285 with or without WO'355 or Schram; and

(4) Claim 11 under 35 U.S.C. §103(a) over WO'355.

Applicants respectfully traverse the above rejections. The applied art does not teach or suggest the claimed invention as set forth below.

As to the §102 rejection, the apparatus described in SU'285 does not disclose the claimed method. Furthermore, WO'355 does not teach that a dielectrophoretic force can be additionally joined with other forces such as ultrasound.

WO'355 describes a method for characterizing particles using dielectrophoresis. It does not describe a particle separation method as in the present application. It does disclose that the particles can be exposed to different fluid parameters such as pH, conductivity and permitivity in addition to the dielectrophoretic force. Although lines 11 to 14 on page 4 of WO'355 states that -

> "Additionally or alternatively, other forces may be used to enhance the movement of the particles. These may include hydrodynamic, ultrasonic, electrophoretic or optical forces."

the specification does not give any teaching whatever as to how these other forces can be applied to provide particle separation. In particular, WO'355 does not teach the methods as claimed by applicants.

SU'285 clearly specifies the use of a stationary standing ultrasound wave. In contrast to this, the claimed invention requires the ultrasonic standing wave to be moving. In the stationary standing wave of the prior art, the spacial locations of the pressure nodes and antinodes remain fixed in time. In the case of a moving wave, sometimes described as a traveling wave, the locations of these nodes change with time.

The geometry of the apparatus described in SU'285 does not permit the production of a traveling ultrasound wave. This can be seen quite simply by looking at the diameter of the chamber specified in SU'285, which diameter is less than

one wavelength of the ultrasound. The chambers used when carrying out the present invention must, in order that they can permit the generation of a traveling wave, have a length of several times the wavelength in question.

Additionally as to SU'285, generating a moving ultrasound wave with respect to the apparatus and method taught therein would, in fact, destroy the separation efficiency of the apparatus described in SU'285, not improve it. As described, the method disclosed in SU'285 depends on the ultrasound forming a pressure node, and hence a concentration of particles, precisely at the location of the central wire electrode in the apparatus described in the specification. The dielectrophoretic force is a maximum at this wire electrode and particle collection by positive dielectrophoresis is said to be enhanced, according to SU'285, by distortion of the electrical double layer surrounding the particles. This would appear to be impossible using the apparatus and method described in SU'285 since dielectrophoresis is sensitive to electrical double layer effects only for electrical field frequencies of less than 1kHz. See Burt et al, (1989) J. Phys. E: Sci. Instrum., Volume 22, pages 952-957 (Abstract attached); and Burt et al, (Biochimica et Biophysica Acta, Volume 1034 (1990), pages 93-101 (a copy attached). The dimensions of the apparatus shown in SU'285 permit ultrasound

frequencies limited to the range of around 1 to 6 MHz (as described in the captioned specification at page 3, lines 17-25; and page 4, lines 16-22) and the separation taught in SU'285 relies on the ultrasound wave and the electric field having exactly the same frequency and phase relationship.

As a consequence of this limitation, in the method described in SU'285, the frequency of the electric field is limited to the range 1 to 6 MHz and this signal has to be matched exactly in frequency and phase with the ultrasound frequency. In contrast, in the claimed method, electric fields are used having frequencies in the range of from at least 1kHz to 10 MHz (page 4, lines 20-26) and these need not be locked in frequency and phase with the ultrasound wave. This enables highly improved efficiency, sensitivity and selectivity of dielectrophoretic particle separation to be achieved relative to that achievable using the apparatus and method described in SU'285.

A further distinction between the method described and claimed in the present application and the disclosures in SU'285 is that the latter requires fluid flow in order to produce particle separation. As explained in the specification of the captioned application, by using a moving ultrasound wave, separation can be achieved in a stationary fluid.

Additionally, the teachings of SU'285 only provide that a small fraction of the particles -- those located in close proximity to the central wire electrode -- i.e., 300 microns or less distance therefrom -- experience a dielectrophoretic force. The vast bulk of the remaining particles are swept through the chamber by the flowing liquid. SU'285 asserts that the effect of the ultrasound is to modulate the strength of the dielectrophoretic force by perturbing the electrical double layer around the particles, but, as indicated above, this does not appear to be consistent with the peer reviewed published art in this field. Accordingly, considerable doubt must be expressed as to whether SU'285 is an enabling disclosure of any sort.

Further, the ultrasound as taught for use in SU'285 is not used physically to extract the particles which are to be moved. The ultrasound also has to be applied at the same time as the electric field.

Schram does not provide for the shortcomings of SU'285 or WO'355. While Schram discloses the use of ultrasonic standing waves to separate different particle types, Schram does not teach or suggest the use of ultrasound waves in combination with dielectrophoresis to enhance particle separation. Further, there is no reason provided in the applied art to combine the ultrasound-based particle separa-

tion methods disclosed in Schram with the dielectrophoretic testing technology disclosed in WO'355. No suggestion is provided in Schram to look any further than using ultrasonic standing waves for separation. Schram achieves separation using ultrasound alone. No motivation is provided to modify the method, much less with a different type of force. Since WO'355 does not provide any teaching as to particle separation, no suggestion can be provided by WO'355 to modify the method taught therein in that regard.

The combination of ultrasonic waves with dielectrophoretic manipulation of particles is critical to the claimed invention and in the absence of hindsight, that the two given techniques could be combined advantageously is not provided in the applied art.

Accordingly, applicants respectfully submit that the claimed invention is not taught or suggested by the applied art within the meanings of 35 U.S.C. §102 and §103. Neither of SU'285 nor WO'355 teaches each and every element of the claimed invention in order to anticipate under §102. Further SU'285, WO'355 and Schram, either alone or in combination, do not provide any suggestion or motivation to modify the teachings therein in such a manner as to provide the claimed invention. Withdrawal of the §102 and §103 rejections is, therefore, respectfully requested.

Reconsideration and allowance of the claims are respectfully urged.

Respectfully submitted,

GARY LOCK ET AL

By _____

Mary J. Breiner, Attorney
Registration No. 33,161
115 North Henry Street
P.O. Box 19290
Alexandria, Virginia 22320-0290

Telephone 703-684-6885

Attachments - Abstract - J. Phys. E: Sci. Instrum., Burt et al (1989), Vol. 22, pp. 952-957
- Biochimica et Biophysica Acta, Burt et al, Vol. 1034 (1990), pp. 93-101